PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61K 31/135, 9/06	A1	(11) International Publication Number: WO 97/04764
		(43) International Publication Date: 13 February 1997 (13.02.97)

(21) International Application Number: PCT/CA96/00505

(22) International Filing Date: 26 July 1996 (26.07.96)

(30) Priority Data:
2,154,979 28 July 1995 (28.07.95) CA

(71)(72) Applicants and Inventors: ARMSTRONG, Kenneth, T. [CA/CA]; Suite 201, 4256 Portage Road, Niagara Falls, Ontario L2E 6A4 (CA). SCHOENHALS, Jennifer, M. [CA/CA]; 6635 Drummond Road, Niagara Falls, Ontario L2G 4N4 (CA).

(74) Agent: RICHES, MCKENZIE & HERBERT; Suite 2900, 2 Bloor Street East, Toronto, Ontario M4W 3J5 (CA).

(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: TOPICAL PHENYLEPHRINE PREPARATION

(57) Abstract

The present invention provides a topical preparation containing a vascoconstricting compound, preferably phenylephrine, for substantially stopping local bleeding from a skin wound. The inventors have found that, when applied to the skin in the vicinity of a bleeding wound, a topical preparation of the present invention will reduce or stop bleeding from the wound by causing vasoconstriction of blood vessels in the skin and the subcutaneous layer. The preparation preferably comprises a cream or ointment containing from about 0.5 to 50 % by weight phenylephrine dispersed in an inert carrier, phenylephrine being present as its hydrochloride.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	**GB**	United Kingdom	**MW**	Malawi
AT	Austria	**GE**	Georgia	**MX**	Mexico
AU	Australia	**GN**	Guinea	**NE**	Niger
BB	Barbados	**GR**	Greece	**NL**	Netherlands
BE	Belgium	**HU**	Hungary	**NO**	Norway
BF	Burkina Faso	**IE**	Ireland	**NZ**	New Zealand
BG	Bulgaria	**IT**	Italy	**PL**	Poland
BJ	Benin	**JP**	Japan	**PT**	Portugal
BR	Brazil	**KE**	Kenya	**RO**	Romania
BY	Belarus	**KG**	Kyrgystan	**RU**	Russian Federation
CA	Canada	**KP**	Democratic People's Republic of Korea	**SD**	Sudan
CF	Central African Republic			**SE**	Sweden
CG	Congo	**KR**	Republic of Korea	**SG**	Singapore
CH	Switzerland	**KZ**	Kazakhstan	**SI**	Slovenia
CI	Côte d'Ivoire	**LI**	Liechtenstein	**SK**	Slovakia
CM	Cameroon	**LK**	Sri Lanka	**SN**	Senegal
CN	China	**LR**	Liberia	**SZ**	Swaziland
CS	Czechoslovakia	**LT**	Lithuania	**TD**	Chad
CZ	Czech Republic	**LU**	Luxembourg	**TG**	Togo
DE	Germany	**LV**	Latvia	**TJ**	Tajikistan
DK	Denmark	**MC**	Monaco	**TT**	Trinidad and Tobago
EE	Estonia	**MD**	Republic of Moldova	**UA**	Ukraine
ES	Spain	**MG**	Madagascar	**UG**	Uganda
FI	Finland	**ML**	Mali	**US**	United States of America
FR	France	**MN**	Mongolia	**UZ**	Uzbekistan
GA	Gabon	**MR**	Mauritania	**VN**	Viet Nam

TOPICAL PHENYLEPHRINE PREPARATION

FIELD OF THE INVENTION

This invention relates to a topical preparation containing a vasoconstricting compound such as phenylephrine for application to the skin in the vicinity of a wound to substantially reduce bleeding from the wound.

BACKGROUND OF THE INVENTION

Human skin is a multilayer structure containing a complex network of blood vessels. The upper layer of the skin, the epidermis, comprises sheets of cells and provides a protective outer layer over the entire body. Beneath the epidermis is the dermis which contains nutritive arteries, veins and capillaries which supply nutrients to the skin. Located below the dermis is a subcutaneous layer containing the venous plexus, which holds large quantities of blood to heat the surface of the skin.

In order to regular skin temperature, arteriovenous (AV) anastomoses are provided in the dermis, comprising large vascular communications directly between the arteries in the dermis and the subcutaneous venous plexus. The AV anastomoses have strong muscular walls innervated by sympathetic vasoconstricting nerve fibres and when constricted, reduce or stop the flow of blood between the arteries of the dermis and the venous plexus.

Although this vasoconstricting effect is most powerful in parts of the body containing AV anastomoses, such as the hands, feet, lips, nose and ears, the skin throughout the body contains sympathetic vasoconstrictor nerve fibres which provide vasoconstrictive control of the nutritive vessels in the dermis.

These sympathetic vasoconstrictor nerve fibres are provided with adrenergic receptors, the two main types of which are classified as alpha receptors and beta receptors. Stimulation of alpha receptors causes vasoconstriction of blood vessels, whereas beta receptor stimulation causes dilation of blood vessels. Drugs which can stimulate either alpha or beta receptors can be used to increase or decrease

blood circulation in the dermis.

Phenylephrine is among known sympathomimetic agents which are believed to stimulate alpha receptors of sympathetic vasoconstrictor nerve fibres and thereby cause vasoconstriction. Phenylephrine is commonly found in over-the-counter preparations for temporary relief of nasal congestion. Its decongesting effect is produced by constriction of the smaller arterioles of the nasal passages. Phenylephrine has also been used in epistaxis (nosebleed) control, and in dentistry and surgery to minimize blood loss during surgical procedures.

Phenylephrine is also known to produce vasoconstriction in the AV anastomoses and nutritive vessels of the skin. However, the disadvantage exists that, to date, neither phenylephrine nor any other vasoconstricting compounds have been used in a topically applied form as a treatment to stop or reduce bleeding from skin wounds, particularly cutaneous bleeding from minor skin wounds.

SUMMARY OF THE INVENTION

To overcome the above disadvantage, the inventors have found that topical application of phenylephrine and other vasoconstricting compounds, as well as physiologically active salts and mixtures thereof, in the vicinity of a bleeding skin wound, can substantially reduce or eliminate the flow of blood from the wound.

Accordingly, the inventors have developed a topical preparation containing at least one vasoconstricting compound as a treatment to substantially reduce or stop bleeding from skin wounds. The most preferred vasoconstricting compound is phenylephrine, which is preferably present in the topical preparation as phenylephrine hydrochloride. Preferably the concentration of the vasoconstricting compound in the topical preparation is from about 0.025% to about 50% by weight, more preferably from about 0.5% to about 50% by weight.

Preferably, the topical preparation of the present invention is in the form of an ointment, cream, or liquid, comprising an effective amount of phenylephrine and a base, the type of base depending on the site of application and reason for use. For example, bases for an ointment or cream may be selected from organogels,

hydrogels and emulsion-type semisolids.

It is one object of the present invention to provide a topical preparation containing a vasoconstricting compound in an amount effective to constrict blood vessels in and below the skin.

It is another object to provide a topical preparation containing a vasoconstricting compound in an amount effective to substantially reduce or stop cutaneous bleeding from a skin wound.

It is another object of the present invention to provide a topical preparation containing phenylephrine in an amount effective to constrict blood vessels in and below the skin.

It is another object of the present invention to provide a topical preparation containing phenylephrine in an amount effective to substantially reduce or stop cutaneous bleeding from a skin wound.

In one aspect, the present invention provides a topical preparation comprising: phenylephrine; and an inert carrier, wherein said phenylephrine is present in said topical preparation in an amount effective to substantially reduce flow of blood from a bleeding skin wound when said topical preparation is applied to said skin wound.

In another aspect, the present invention provides a topical composition for stemming the flow of blood from a skin wound, comprising: phenylephrine; and an inert carrier.

Preferably, phenylephrine is present in the above topical preparation and composition in an amount effective to substantially stop cutaneous bleeding from minor skin wounds.

In yet another aspect, the present invention provides a method for treatment of a skin wound to substantially reduce bleeding therefrom, said method comprising: applying a topical preparation comprising phenylephrine in an inert carrier to the skin wound.

Preferably, the topical preparation and composition of the present invention is further applied directly to the wound and to an area of skin surrounding the

wound.

Use of the topical preparation and composition of the present invention preferably causes cutaneous bleeding from a skin wound to be substantially stopped.

In topical preparations and compositions of the present invention, the inert carrier is preferably selected from a group comprising organogels, hydrogels and emulsion-type semisolids.

BRIEF DESCRIPTION OF THE DRAWINGS

Further aspects and advantages of the present invention will become apparent from the following description, taken together with the accompanying drawing, in which:

Figure 1 is a sectional, schematic diagram illustrating the structure of human skin and blood circulation therein.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Preferred embodiments of the invention are now described with reference to Figure 1.

Figure 1 is a schematic diagram showing a sectional view of the structure of human skin. As shown in Figure 1, skin comprises an upper epidermis 10 which contains layers of skin cells and provides the body with an outer protective barrier.

Under the epidermis 10 is the dermis 12, which contains the nutritive blood vessels of the skin. Figure 1 illustrates these nutritive vessels as comprising arteries 14, veins 16 and capillaries 18.

Under the dermis 12 is the subcutaneous layer 20 which contains the venous plexus 22, shown in Figure 1 as an intricate network of blood vessels.

The arteries 14 of the dermis 12 communicate with the venous plexus 22 of the subcutaneous tissue 20 by means of AV anastomoses 24.

As discussed above, the blood vessels 14, 16 and 18 of the dermis 12 and the AV anastomoses 24 have alpha-adrenergic receptors which may be caused to constrict by sympathomimetic agents, thereby restricting or cutting off blood flow

to and/or in the blood vessels 14, 16 and 18 of the dermis 12 and between the arteries 14 and the venous plexus 22.

In the topical preparation of the present invention, phenylephrine, or (R)-3-hydroxy-alpha-[(methylamino)methyl] benzenemethanol, is applied to the skin and is believed to stimulate adrenergic alpha receptors in the AV anastomoses 24 and the nutritive vessels 14, 16 and 18, thereby causing vasoconstriction of the AV anastomoses 24, and the blood vessels 14, 16 and 18 in the dermis 12.

When applied to the skin in the vicinity of a skin wound, the topical preparation of the present invention substantially reduces, and preferably completely stops, bleeding from the wound.

The term "skin wound" as used herein refers to wounds which penetrate the upper epidermis 10 and cause damage to blood vessels 14, 16 and 18 in the dermis, resulting in the flow of blood from the wound. A skin wound may also damage the AV anastomoses 24 and the venous plexus 22 of the subcutaneous layer 20. Types of skin wounds include cuts, punctures and scrapes. Preferably, the topical preparation of the present invention is used on skin wounds of a minor nature.

Preferably, the topical preparation according to the present invention may be used to substantially reduce or completely stop cutaneous bleeding from a minor skin wound. The term "cutaneous bleeding" refers to blood flow from the blood vessels 14, 16 and 18 of the dermis 12.

Preferably, the topical preparation of the present invention is used on skin wounds of humans, although it may be used on other mammals such as dogs.

To stop or substantially reduce bleeding, the topical preparation of the present invention is applied in the vicinity of the wound, meaning the wound itself and the skin immediately surrounding the wound.

Phenylephrine, due to its cost and effectiveness, is the most preferred active ingredient of the topical preparation of the present invention, causing vasoconstriction of the blood vessels in the vicinity of the wound, thereby substantially reducing or completely stopping bleeding from the wound. Other vasoconstricting compounds which may be used as active ingredients include

phenylethylamine, epinephrine, norepinephrine, dopamine, nordefrin, isoproterenol, isoetharine, metaproterenol, terbutaline, fenoterol, metaraminol, tyramine, nylidrin, isoxuprine, ritodrine, methoxyphenamine, methoxamine, soterenol, benzphetamine, ephedrine, phenylpropanolamine, phentermine, chlorphentermine, naphazoline, tetrahydrozoline, oxymetazoline, xylometazoline, tuaminoheptane, cyclopentamine, propylhexadrine, pseudoephedrine, pharmaceutically acceptable salts of said vasoconstricting compounds, and mixtures thereof.

The stoppage of blood flow by the topical preparation of the present invention can be of great value in preventing substantial loss of blood from a wound.

The topical preparation according to the present invention comprises a vasoconstricting effective amount of a vasoconstricting compound dispersed in an inert carrier. Preferably, the vasoconstricting compound is present in the topical preparation in an amount of about 0.025 to about 50% by weight, and more preferably about 0.5 to about 50% by weight of the preparation. Preferably, the amount of phenylephrine in the preparation is effective to reduce or stop blood flow in less than about five minutes. The most preferred topical preparation of the present invention contains phenylephrine in an amount of about 2 to about 6% w/w, with about 5% w/w being particularly preferred.

It is to be appreciated that preparations containing smaller concentrations of phenylephrine may preferably be used to reduce or stop cutaneous bleeding from minor skin wounds and may require a longer time to reduce or stop bleeding, whereas preparations containing higher concentrations of phenylephrine may preferably be used to stop or reduce bleeding from more serious wounds and result in faster reduction or stoppage of bleeding.

Most preferably, phenylephrine is present in the topical preparation in the form of a physiologically active salt, the hydrochloride being most preferred. However, it is to be understood that other forms of phenylephrine may also be suitable, such as other physiologically active salts.

Preferred forms of topical preparations include creams, ointments, lotions,

shampoos, aerosols, gels and liquids. Topical preparations according to the present invention may also be incorporated into pads or wound dressings.

The topical preparation according to the present invention is more preferably in the form of a cream or ointment. The inert carrier is preferably a base which may comprise one or more compounds selected from a number of groups of substances, including organogels, hydrogels, emulsion-type semisolids and emulsified bases. A particularly preferred base comprises about 45 to 50% Dermobase™, about 45 to 50% Aquaderm™, and about 0 to 5% distilled water, the amounts being expressed in terms of percent by volume of the base.

Preferred organogels include hydrocarbon type organogels such as those selected from the group comprising petrolatum and mineral oil-polyethylene gels; animal and vegetable fats such as those selected from the group comprising lard, hydrogenated vegetable oils and theobroma oil; soap base greases such as those selected from the group comprising aluminum stearate and mineral oil gels; and hydrophilic organogels such as those selected from the group comprising carbowax bases and polyethylene glycol ointment.

Preferred hydrogels include organic hydrogels such as those selected from the group comprising pectin paste and tragacanth jelly, and inorganic hydrogels such as those selected from the group comprising bentonite gels and colloidal magnesium aluminum silicate gels.

Preferred emulsion-type semisolids include water-in-oil emulsifiable bases and oil-in-water emulsifiable bases selected from the group comprising hydrophillic petrolatum, wool fat, and anhydrous Tween base (white petrolatum, stearyl alcohol, glycerine and tween 60). Preferred emulsion-type semisolids also include emulsified bases such as water-in-oil emulsified bases and oil-in-water emulsified bases, such as those selected from the group comprising hydrous wool fat, rose water ointment, hydrophillic ointment and vanishing cream.

A preferred method of preparing a topical phenylephrine preparation according to the present invention comprises reducing the vasoconstricting compound to an impalpable powder by levigating it with an equal amount of water.

The base is then added incrementally using geometric dilution using a spatula on a hard surface (such as an ointment pad).

A number of trials were conducted to test the efficacy of topical preparations of the present invention in humans and other mammals. The results of some of these trials are presented in the following examples, in which the subjects are human unless otherwise indicated.

Example 1

Subject: Male

Age Range: 36-50

Location(s) of Laceration(s): Neck, chin.

Type(s) of Laceration(s): Cuts from shaving.

Number of Applications: 8

Form of Topical Preparation: Cream containing 5% w/w phenylephrine hydrochloride.

Time Required to Stop Bleeding: Stopped immediately after application.

Side Effects: None.

Example 2

Subject: Male

Age Range: 36-50

Location(s) of Laceration(s): Hands and face.

Type(s) of Laceration(s): Cuts from shaving and skinned knuckles resulting in detachment of a flap of skin.

Number of Applications: 5

Form of Topical Preparation: As in Example 1.

Time Required to Stop Bleeding: 10-20 seconds.

Side Effects: None.

Example 3

Subject: Male

Age Range: 26-35

Location(s) of Laceration(s): Face.

Type(s) of Laceration(s): Cuts, close to surface.

Number of Applications: 10-15

Form of Topical Preparation: As in Example 1.

Time Required to Stop Bleeding: 5-10 seconds.

Side Effects: None.

Example 4

Subject: Female

Age Range: 26-35

Location(s) of Laceration(s): Leg.

Type(s) of Laceration(s): Cut, close to surface.

Number of Applications: 1

Form of Topical Preparation: As in Example 1.

Time Required to Stop Bleeding: 30-60 seconds.

Side Effects: None.

Example 5

Subject: Male

Age Range: 51-65

Location(s) of Laceration(s): Face and neck.

Type(s) of Laceration(s): Shaving lacerations.

Number of Applications: 10

Form of Topical Preparation: As in Example 1.

Time Required to Stop Bleeding: 1 minute.

Side Effects: None.

Comments: Subject takes aspirin daily as a blood thinner.

Example 6

Subject: Male

Age Range: 36-50

Location(s) of Laceration(s): Face and hands.

Type(s) of Laceration(s): Cuts from shaving, lacerations to hand.

Number of Applications: 50

Form of Topical Preparation: As in Example 1.

Time Required to Stop Bleeding: 1 minute for facial cuts; 3-5 minutes for deeper hand cuts.

Side Effects: Moisturization of skin.

Example 7

Subject: Male

Age Range: 36-50

Location(s) of Laceration(s): Face.

Type(s) of Laceration(s): Scrapes.

Number of Applications: 3

Form of Topical Preparation: Ointment containing 5% w/w phenylephrine hydrochloride.

Time Required to Stop Bleeding: Short time.

Side Effects: None.

Example 8

Subject: Male

Age Range: Under 25

Location(s) of Laceration(s): Face and scalp.

Type(s) of Laceration(s): Puncture wounds, lacerations up to 1 cm long, shaving cuts, bleeding pimples.

Number of Applications: 12

Form of Topical Preparation: As in Example 7.

Time Required to Stop Bleeding: Less than 1 minute.

Side Effects: Temporary whitening of skin in area around a pimple to which preparation was applied.

Example 9

Subject: Male dog

Age Range: --

Location(s) of Laceration(s): Scrotum.

Type(s) of Laceration(s): Surface abrasion with slow seepage of blood.

Number of Applications: 3

Form of Topical Preparation: Liquid containing 3% w/w phenylephrine hydrochloride.

Time Required to Stop Bleeding: 3 minutes.

Side Effects: Nothing obvious.

Example 10

Subject: Dogs

Age Range: --

Location(s) of Laceration(s): Feet, ear flap.

Type(s) of Laceration(s): Toenails cut too short, blood vessel exposed "end-on"; puncture and cut in ear flap.

Number of Applications: 4-5

Form of Topical Preparation: Ointment and liquid containing 4-5% w/w phenylephrine hydrochloride.

Time Required to Stop Bleeding: Bleeding not stopped.

Side Effects: None.

Example 11

Subject: Male

Age Range: Under 25

Location(s) of Laceration(s): Neck.

Type(s) of Laceration(s): Cut, close to surface.

Number of Applications: 5

Form of Topical Preparation: As in Example 1.

Time Required to Stop Bleeding: 1-2 minutes.

Side Effects: None.

Example 12

Subject: Male

Age Range: 26-35

Location(s) of Laceration(s): Legs.

Type(s) of Laceration(s): Scrapes, abrasions.

Number of Applications: 10

Form of Topical Preparation: As in Example 7.

Time Required to Stop Bleeding: 30-40 seconds.

Side Effects: None.

Example 13

Subject: Female

Age Range: 26-35

Location(s) of Laceration(s): Hand.

Type(s) of Laceration(s): Cut, close to surface.

Number of Applications: 1

Form of Topical Preparation: As in Example 1.

Time Required to Stop Bleeding: Few minutes.

Side Effects: Burning.

Example 14

Subject: Male

Age Range: 26-35

Location(s) of Laceration(s): Legs.

Type(s) of Laceration(s): Scrapes, abrasions.

Number of Applications: 10

Form of Topical Preparation: As in Example 7.

Time Required to Stop Bleeding: 30-40 seconds.

Side Effects: None.

Example 15

Subject: Male

Age Range: 36-50

Location(s) of Laceration(s): Neck.

Type(s) of Laceration(s): Shaving cut.

Number of Applications: 1

Form of Topical Preparation: As in Example 1.

Time Required to Stop Bleeding: Less than 1 minute.

Side Effects: N/A.

Example 16

Subject: Male

Age Range: 80

Location(s) of Laceration(s): Arm.

Type(s) of Laceration(s): 5 cm flap laceration.

Number of Applications: 1

Form of Topical Preparation: As in Example 7.

Time Required to Stop Bleeding: Two minutes.

Side Effects: N/A.

Comments: The laceration bled continuously for about 48 hours prior to application of the topical preparation.

Example 17

Subject: Male

Age Range: N/A

Location(s) of Laceration(s): Upper lip.

Type(s) of Laceration(s): cut sustained during karate match.

Number of Applications: 1

Form of Topical Preparation: As in Example 7.

Time Required to Stop Bleeding: One to two minutes.

Side Effects: N/A.

The results of the above examples are generally favourable, with bleeding generally being stopped within a few minutes and few side effects being reported. All human subjects reported that they would use the product again, and most reported that the topical preparation of the present invention is superior to other products on the market to stop bleeding.

Topical preparations of the present invention, particularly those containing 5% by weight phenylephrine, have been found to be particularly effective to stop bleeding from facial lacerations sustained in sport fighting, such as karate and boxing. Preferably, such preparations are in the form of an ointment. During such boxing or karate matches, participants may be disqualified for sustaining a bleeding laceration. It has been found that the most preferred topical preparation according to the present invention containing 5% by weight phenylephrine effectively stops bleeding from such lacerations within about one to two minutes, thus allowing the participant to continue fighting. Furthermore, before a sport fighting match, participants may apply the topical preparation of the present invention to the most cut-prone areas of the body, such as the face, to prevent bleeding in the event that the skin is lacerated.

In experiments conducted by the inventors, no infection of wounds treated with the topical preparation of the present invention has been observed, and wounds have been observed to heal quickly with minimal scarring. Furthermore, the inventors

have found that the most preferred topical preparation containing phenylephrine stops bleeding quickly without any pain.

In addition, the inventors have found that the topical preparation according to the present invention is effective for treating minor injuries other than cuts and lacerations. For example, topical preparations of the present invention containing phenylephrine have been found to reduce the itch and irritation caused by insect bites, for example from mosquitos, and also to minimize the swelling associated with such insect bites. Topical preparations containing phenylephrine have also been found to be effective in treating "razor burn", which is minor facial irritation associated with shaving. In addition, the topical preparation may be applied to the facial area prior to shaving to prevent razor burn and to prevent bleeding from minor shaving cuts. For treatment of insect bites and razor burn, the topical preparation of the present invention is preferably in the form of a cream.

Although the invention has been described with reference to certain preferred embodiments, it is to be understood the invention includes all embodiments which are within the scope of the following claims.

WE CLAIM:

1. A topical preparation comprising:

phenylephrine; and

an inert carrier,

wherein said phenylephrine is present in said topical preparation in an amount effective to substantially reduce flow of blood from a bleeding skin wound when said topical preparation is applied to said skin wound.

2. The topical preparation of claim 1, wherein phenylephrine is present in an amount effective to substantially stop cutaneous bleeding from minor skin wounds.

3. The topical preparation of claim 1, wherein the inert carrier is selected from a group comprising organogels, hydrogels and emulsion-type semisolids.

4. The topical preparation of claim 1, wherein phenylephrine comprises from about 0.5% to 50% by weight of the preparation.

5. The topical preparation of claim 1, wherein phenylephrine is present in the preparation of phenylephrine hydrochloride.

6. A topical composition for stemming the flow of blood from a skin wound, comprising:

phenylephrine; and

an inert carrier.

7. The topical composition of claim 6, wherein phenylephrine is present in an amount effective to substantially stop cutaneous bleeding from minor skin wounds.

8. The topical composition of claim 6, wherein the inert carrier is selected from

a group comprising organogels, hydrogels and emulsion-type semisolids.

9. The topical composition of claim 6, wherein phenylephrine comprises from about 0.5% to 50% by weight of the composition.

10. The topical composition of claim 6, wherein phenylephrine is present in the composition as phenylephrine hydrochloride.

11. The topical composition of claim 10, wherein phenylephrine hydrochloride comprises about 5% by weight of the composition.

12. A topical preparation comprising:

a vasoconstricting compound; and

an inert carrier,

wherein said vasoconstricting compound is present in said topical preparation in an amount effective to substantially reduce flow of blood from a bleeding skin wound when said topical preparation is applied to said skin wound.

13. The topical preparation of claim 12, wherein said vasoconstricting compound is present in an amount effective to substantially stop cutaneous bleeding from minor skin wounds.

14. The topical preparation of claim 12, wherein the inert carrier is selected from a group comprising organogels, hydrogels and emulsion-type semisolids.

15. The topical preparation of claim 12, wherein said vasoconstricting compound comprises from about 0.025% to 50% by weight of the preparation.

16. The topical composition of claim 15, wherein said vasoconstricting compound comprises from about 0.5% to 50% by weight of the composition.

17. The topical preparation of claim 12, wherein said vasoconstricting compound is selected from the group comprising phenylethylamine, epinephrine, norepinephrine, dopamine, nordefrin, isoproterenol, isoetharine, metaproterenol, terbutaline, fenoterol, metaraminol, phenylephrine, tyramine, nylidrin, isoxuprine, ritodrine, methoxyphenamine, methoxamine, soterenol, benzphetamine, ephedrine, phenylpropanolamine, phentermine, chlorphentermine, naphazoline, tetrahydrozoline, oxymetazoline, xylometazoline, tuaminoheptane, cyclopentamine, propylhexadrine, pseudoephedrine, pharmaceutically acceptable salts of said vasoconstricting compounds, and mixtures thereof.

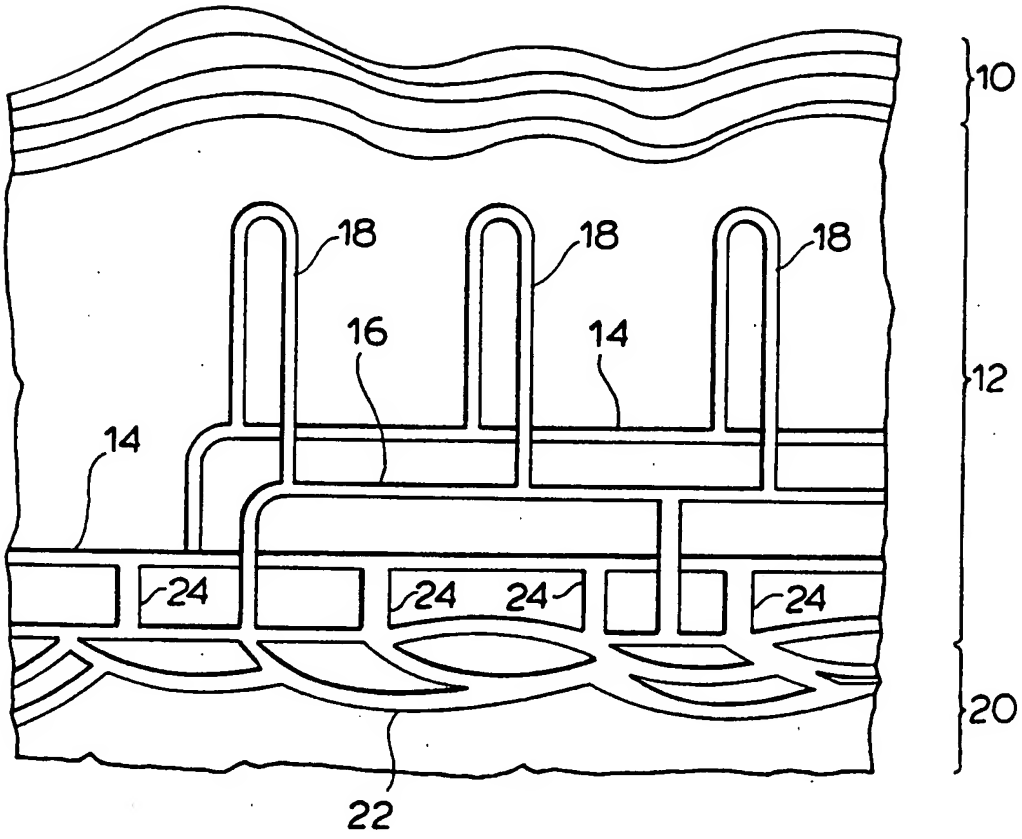

FIG. 1.

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/CA 96/00505

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K31/135 A61K9/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US,A,5 395 318 (E.K.KAPRELIAN) 7 March 1995 see claims 11-17 ---	1-17
Y	WO,A,93 07902 (RICHARDSON-VICKS) 29 April 1993 see the whole document ---	1-17
Y	EP,A,0 521 455 (TAKEDA) 7 January 1993 see claims see page 4, line 9 - line 10 ---	1-17
Y	US,A,5 420 197 (D.H.LORENZ ET AL.) 30 May 1995 see claims 1,5,17,18,28 --- -/--	1-17

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

1

Date of the actual completion of the international search	Date of mailing of the international search report
15 November 1996	22.11.96

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Scarponi, U

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Int ional Application No
PCT/CA 96/00505

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y,P	US,A,5 453 445 (R.A.HENRY) 26 September 1995 see the whole document ---	1-17
Y,P	DATABASE WPI Week 9618 Derwent Publications Ltd., London, GB; AN 96-175678 [18] XP002018645 A, see abstract & JP,A,08 053 368 (KYOTO YAKUHIN KOGYO KK) 27 February 1996 -----	1-17

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

information on patent family members

Inter nal Application No
PCT/CA 96/00505

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US-A-5395318	07-03-95	NONE		
WO-A-9307902	29-04-93	AU-A-	2806492	21-05-93
		BR-A-	9206632	25-04-95
		CA-A-	2120927	29-04-93
		CN-A-	1072863	09-06-93
		CZ-A-	9400859	15-12-94
		EP-A-	0608320	03-08-94
		FI-A-	941771	15-04-94
		JP-T-	7500113	05-01-95
		NO-A-	941319	16-06-94
		PT-A-	100963	29-10-93
		SK-A-	43294	05-01-95
EP-A-521455	07-01-93	CA-A-	2072812	03-01-93
		JP-A-	5294824	09-11-93
US-A-5420197	30-05-95	AU-A-	8038294	20-07-95
		CA-A-	2138351	14-07-95
		EP-A-	0663212	19-07-95
		JP-A-	7250886	03-10-95
US-A-5453445	26-09-95	US-A-	5534242	09-07-96